SCIENTIFIC ABSTRACT:

Allogeneic transplant is the only curative therapy for the stem cell malignancy CML. However, allogeneic transplants are available to only 25-30% of CML patients affected because of lack of a suitably matched donor or because of age. Benign stem cells coexist with the malignant clone in most patients with CML. Autologous transplantation may therefore be an alternative treatment modality. However, autologous transplants have not yet proven curative in part due to the fact that "purging" of the massively contaminated marrow and/or blood is inefficient. in 2 sequential ABMT studies at the University of Minnesota, we have evaluated the effectiveness of ex vivo purging with γ-interferon, in vivo mobilization with cyclophosphamide and GM-CSF and in vivo priming with Cyclophosphamide, Mitoxantrone and Cytosine Arabinoside and G-CSF to obtain long-lasting benign hematopoiesis in CML. However, although early recovery of non-malignant hematopoiesis was seen in a fraction of patients, we have demonstrated that γ-interferon purging results in a significant toxicity against the normal stem cell compartment resulting in failure to engraft in 25% of patients. Furthermore, the majority of patients had recovery of Ph+ hematopoiesis. Similarly, transplantation with in vivo mobilized BM or PBPC stem cell populations resulted in only a minority of patients in Ph negative hematopoiesis. Therefore, to examine if "infused malignant progenitors contribute to post transplant relapse?" we will retrovirally mark 25% of the PBPC inoculum obtained after priming with a NEO marker. We will therefore perform autologous transplants with retrovirally marked PBPC cells, enriched for CD34+ cells, obtained after cyclophosphamide G-CSF mobilization in CML. The retroviral marker will allow us to determine the contribution of infused malignant cells to post transplant relapse.